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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/737,262	
	Filing Date	12/15/03
	First Named Inventor	Leonidas Stefanis
	Art Unit	1632
	Examiner Name	to be assigned
Attorney Docket Number	5199-26	
Total Number of Pages in This Submission	20	

ENCLOSURES (Check all that apply)

<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance communication to Technology Center (TC)
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment/Reply	<input type="checkbox"/> Petition	<input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
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<input type="checkbox"/> Response to Missing Parts/Incomplete Application	Remarks	
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Todd Holmbo, Reg. No. 42,665
Signature	
Date	7/26/04

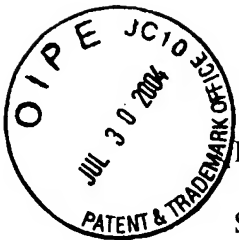
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Leonidis Stefanis, et al., Docket No.: 5199-26
Serial No.: 10/737,262 Examiner: to be assigned
Filed: December 15, 2003 Group Art Unit: 1632
Title: **DOPAMINERGIC CELL LINES STABLY EXPRESSING A53T
ALPHA-SYNUCLEIN AND METHODS OF USING SAME**

July 26, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.97(b)

Sir:

In accordance with the duty of disclosure under 37 CFR §1.56, applicant hereby notifies the U. S. Patent and Trademark Office of the following documents, which are listed on the attached PTO/SB/08B form. The examiner may deem these documents to be relevant to patentability of the claims of the above-identified application. A Copy of the document is enclosed for the examiner's convenience.

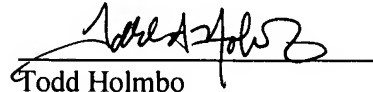
The submission of the listed documents is not intended as an admission that any of the documents constitute prior art against the claims of the present application. Applicants do not waive any right to take any action that would be appropriate to antedate or otherwise remove any listed document as a competent reference against the claims of the present application.

Applicants respectfully request that the listed documents be considered by the examiner and be made of record in the present application and that initialed a copy of form PTO/SB/08B be returned in accordance with MPEP §609.

It is understood that no fee is necessary for submission of this Information Disclosure Statement, as it is being filed before the later of three months from the filing date or the mailing of the first Office Action on the merits.

The Commissioner is hereby authorized to charge payment of any fees associated with this application or credit any overpayment to Deposit Account No. 02-4270.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Todd Holmbo", written over a horizontal line.

Todd Holmbo

Reg. No. 42,665

Attorney for Applicants

BROWN RAYSMAN MILLSTEIN

FELDER & STEINER LLP

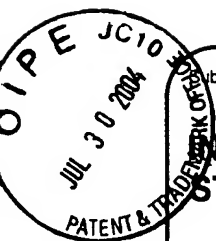
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known	
		Application Number	10/737,262
		Filing Date	12/15/03
		First Named Inventor	Leonidas Stefanis
		Art Unit	1632
		Examiner Name	to be assigned
Sheet 1	of 17	Attorney Docket Number	5199-26

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Ancolio et al., alpha-Synuclein and the Parkinson's disease-related mutant Ala53Thr-alpha-synuclein do not undergo proteasomal	
		degradation in HEK293 and neuronal cells.	
		Neurosci. Lett., 285: 79-82, 2000	
		Anglade et al., Apoptosis and autophagy in nigral neurons of patients with Parkinson's disease.	
		Histol. Histopathol., 12: 25-31, 1997	
		Baba et al., Aggregation of alpha-synuclein in Lewy bodies of sporadic Parkinson's disease and dementia with Lewy bodies.	
		Am. J. Pathol., 152: 879-884, 1998	
		Brunk et al., Exposure of cells to nonlethal concentrations of hydrogen peroxide induces degeneration-repair mechanisms involving lysosomal	
		destabilization.	
		Free Radic. Biol. Med., 19: 813-822, 1995	

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet	2	of	17	Attorney Docket Number	5199-26
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NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Burke, Apoptosis in degenerative diseases of the basal ganglia.	
		The Neuroscientist, 4: 301-311, 1998	
		Bursch et al., programmed cell death (PCD). Apoptosis, autophagic PCD, or others?	
		Ann. NY Acad. Sci., 926: 1-12, 2000	
		Cavanagh et al., Routes of excretion of neuronal lysosomal dense bodies after ventricular infusion of leupeptin in the rat: a study using ubiquitin and	
		PGP 9.5 immunocytochemistry.	
		J. Neurocytol., 22: 779-791, 1993	
		Ciechanover, The ubiquitin-proteasome pathway: on protein death and cell life.	
		EMBO J., 17: 7151-7160, 1998	

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		Application Number	10/737,262
		Filing Date	12/15/03
		First Named Inventor	Leonidas Stefanis
		Art Unit	1632
		Examiner Name	to be assigned
Sheet 3	of 17	Attorney Docket Number	5199-26

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Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Clayton and George, The synucleins: a family of proteins involved in synaptic function, plasticity, neurodegeneration, and disease.	
		Trends Neurosci., 21: 249-254, 1998	
		Clayton and George, Synucleins in synaptic plasticity and neurodegenerative disorders.	
		J. Neurosci. Res., 58: 120-129, 1999	
		Clarke, Developmental cell death: morphological diversity and multiple mechanisms.	
		Anat. Embryol. (Berl), 181: 195-213, 1990	
		Conway et al., Accelerated in vitro fibril formation by a mutant alpha-synuclein linked to early-onset Parkinson disease.	
		Nat. Med., 11: 1318-1320, 1998	
		Fahn and Przedborski, Parkinsonism. In: Merritt's textbook of neurology, Ed 10 (Rowland LP, ed), pp 679-693. Philadelphia: Williams & Wilkins 2000	

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		Application Number	10/737,262
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		First Named Inventor	Leonidas Stefanis
		Art Unit	1632
		Examiner Name	to be assigned
Sheet 4	of 17	Attorney Docket Number	5199-26

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		Figueiredo-Pereira et al., A new inhibitor of the chymotrypsin-like activity of the multicatalytic proteinase complex (20S proteasome) induces	
		accumulation of ubiquitin-protein conjugates in a neuronal cell.	
		J. Neurochem., 63: 1578-1581, 1994	
		Fon et al., Vesicular transport regulates monoamine storage and release but is not essential for amphetamine action.	
		Neuron, 19: 1271-1283, 1997	
		Forno and Norville, Ultrastructure of Lewy bodies in the stellate ganglion.	
		Acta. Neuropathol. (Berl), 34: 183-197, 1976	
		Furlong et al., Alpha-synuclein over expression promotes aggregation of mutant huntingtin.	
		Biochem. J., 15: 577-581, 2000	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)	Application Number		10/737,262
	Filing Date		12/15/03
	First Named Inventor		Leonidas Stefanis
	Art Unit		1632
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Sheet 5	of 17	Attorney Docket Number 5199-26	

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		Ghee et al., Rat alpha-synuclein interacts with tat binding protein 1, a component of the 26S proteasomal complex.	
		J. Neurochem., 75: 2221-2224, 2000	
		Goldstein and Greene, Activation of tyrosine hydroxylase by phosphorylation. In: Psychopharmacology: a third generation of progress	
		(Meltzer H, ed), pp 75-80. New York: Raven, 1987	
		Greene and Tischler, Establishment of a noradrenergic clonal line of rat adrenal pheochromocytoma cells which respond to nerve growth factor.	
		Proc. Natl. Acad. Sci. USA 73: 2424-2428, 1976	
		Greene, et al., Culture and experimental use of the PC12 rat pheochromocytoma cell line. In: Culturing nerve cells (Banker G, Goslin K, eds), pp 161-189.	
		Cambridge, MA: MIT Press, 1998; Stefanis et al., 2001, supra).	
		Hornykiewicz, Dopamine (3-hydroxytyramine) and brain function.	
		Pharmacol. Rev., 18: 925-965, 1996	

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				Filing Date	12/15/03
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		Hsu et al., Alpha-Synuclein promotes mitochondrial deficit and oxidative stress.	
		Am. J. Pathol., 157: 401-410, 2000	
		Imai et al., An unfolded putative transmembrane polypeptide, which can lead to endoplasmic reticulum stress, is a substrate of Parkin.	
		Cell, 105: 891-902, 2001	
		Kanda et al., Enhanced vulnerability to oxidative stress by alpha-synuclein mutations and C-terminal truncation.	
		Neuroscience, 97: 279-284, 2000	
		Kegel et al., Huntingtin expression stimulates endosomal-lysosomal activity, endosome tabulation, and autophagy.	
		J. Neurosci., 20: 7268-7278, 2000	
		Kitada et al., Mutations in the parkin gene cause autosomal recessive juvenile parkinsonism.	
		Nature, 392: 605-608, 1998	

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		Leroy et al., The ubiquitin pathway in Parkinson's disease.	
		Nature, 395: 451-452, 1998	
		Masliah et al., Dopaminergic loss and inclusion body formation in alpha-synuclein mice: implications for neurodegenerative disorders.	
		Science, 287: 1265-1269, 2000	
		Matsuoka et al., Lack of nigral pathology in transgenic mice expressing human alpha-synuclein driven by the tyrosine hydroxylase promoter.	
		Neurobiol. Dis., 8: 535-539, 2001	
		Mayer et al., Ubiquitin, lysosomes, and neurodegenerative diseases.	
		Ann. NY Acad. Sci., 674: 149-160, 1992	
		McNaught and Jenner, Proteasomal function is impaired in substantia nigra in Parkinson's disease.	
		Neurosci. Lett., 297: 191-194, 2001	

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Sheet 8	of 17	Attorney Docket Number	5199-26

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		McNaught et al., Failure of the ubiquitin-proteasome system in Parkinson's disease.	
		Nat. Rev. Neurosci., 2: 589-594, 2001	
		Neystat, et al., Alpha-synuclein expression in substantia nigra and cortex in Parkinson's disease.	
		Mov. Disord., 14: 417-422, 1999	
		Ohsawa et al., An ultrastructural and immunohistochemical study of PC12 cells during apoptosis induced by serum deprivation with special reference	
		to autophagy and lysosomal cathepsins.	
		Arch. Histol. Cytol., 61: 395-403, 1998	
		Ohtani-Kaneko et al., Proteasome inhibitors which induce neurite outgrowth from PC12h cells cause different subcellular accumulations of	
		multi-ubiquitin chains.	
		Neurochem. Res., 23: 1435-1443, 1998	

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STATEMENT BY APPLICANT**

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)	Application Number		10/737,262
	Filing Date		12/15/03
	First Named Inventor		Leonidas Stefanis
	Art Unit		1632
	Examiner Name		to be assigned
Sheet 9	of 17	Attorney Docket Number 5199-26	

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Ostrerova et al., Alpha-Synuclein shares physical and functional homology with 14-3-3 proteins.	
		J. Neurosci., 19: 5782-5791, 1999	
		Ostrerova-Golts et al., The A53T alpha-synuclein mutation increases iron-dependent aggregation and toxicity.	
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		Papadimitriou et al., Mutated alpha-synuclein gene in two Greek kindreds with familial PD: incomplete penetrance? Neurology, 52: 651-654, 1999	
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		Science, 276: 2045-2047, 1997	
		Pothos et al., Synaptic vesicle transporter expression regulates vesicle phenotype and quantal size.	
		J. Neurosci., 20: 7297-7306, 2000	

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		Rathke-Hartlieb et al., Sensitivity to MPTP is not increased in Parkinson's disease-associated mutant-synuclein transgenic mice.	
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		Seglen et al., Structural aspects of autophagy.	
		Adv. Exp. Med. Biol., 389: 103-111, 1996	

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		Shimura et al., Ubiquitination of a new form of alpha-synuclein by parkin from human brain: implications for parkinson's disease.	
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		Shimura et al., Familial Parkinson disease gene product, parkin, is an ubiquitin-protein ligase.	
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		Stefanis et al., Synuclein 1 is selectively upregulated in response to NGF treatment in PC12 cells.	
		J. Neurochem., 76: 1165-1176, 2001	

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of

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		Stefanis et al., Caspase-2 (Nedd2) processing and death of trophic factor-deprived PC12 cells and sympathetic neurons occur independently	
		of caspase-3 (CPP-32)-like activity.	
		J. Neurosci., 18: 9204-9215, 1998	
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		Tabrizi et al., Expression of mutant alpha-synuclein causes increased susceptibility to dopamine toxicity.	
		Hum. Mol. Genet., 9: 2683-2689, 2000	
		Tanaka et al., Inducible expression of mutant alpha-synuclein decreases proteasome activity and increases sensitivity to mitochondria-dependent	
		apoptosis.	
		Hum. Mol. Genet., 10: 919-926, 2001	

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		Tennyson et al., Structural abnormalities associated with congenital megacolon in transgenic mice that overexpress the Hoxa-4 gene.	
		Dev. Dyn., 98: 128-153, 1993	
		Tischler, et al., Morphological and cytochemical properties of a clonal line of rat adrenal pheochromocytoma cells which respond to nerve growth factor.	
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		Eur. J. Cell. Biol., 71: 311-318, 1996	

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		Xue et al., Autophagy is activated by apoptotic signaling in sympathetic neurons: an alternative mechanism of death execution.	
		Mol. Cell. Neurosci., 14: 180-198, 1999	
		Zhou et al., Over expression of human alpha-synuclein causes dopamine neuron death in rat primary culture and immortalized mesencephalon-	
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		J. Biol. Chem., 274: 33855-33858, 1999	

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		Drexler, Activation of the cell death program by inhibition of proteasome function.	
		Proc. Natl. Acad. Sci., USA, 94: 855-860, 1997	
		Giasson et al., Mutant and wild type human alpha-synucleins assemble into elongated filaments with distinct morphologies in vitro.	
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		J. Biol. Chem., 276: 35661-35664, 2000	

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		J. Biol.Chem., 272: 12893-12896, 1997	
		Mesner et al., Nerve growth factor withdrawal-induced cell death in neuronal PC12 cells resembles that in sympathetic neurons.	
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		J. Biol. Chem., 274: 11789-11795, 1999	
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		Proc. Natl. Acad. Sci. USA, 95: 6469-6473, 1998	

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		J. Biol. Chem., 271: 30663-30671, 1996	
		Ueda, et al., Molecular cloning of cDNA encoding an unrecognized component of amyloid in Alzheimer's Disease.	
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		CDCrel-1.	
		Proc. Natl. Acad. Sci. USA, 97: 13354-13359, 2000	

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